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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/595,275

04/04/2006

Masaya Nakatani

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EXAMINER

KASTEN, ROBERT J

ART UNIT

PAPER NUMBER

1795

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/595,275	<b>Applicant(s)</b> NAKATANI ET AL.	
	<b>Examiner</b> ROBERT KASTEN	<b>Art Unit</b> 1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7-19 and 34-43 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-19 and 34-43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

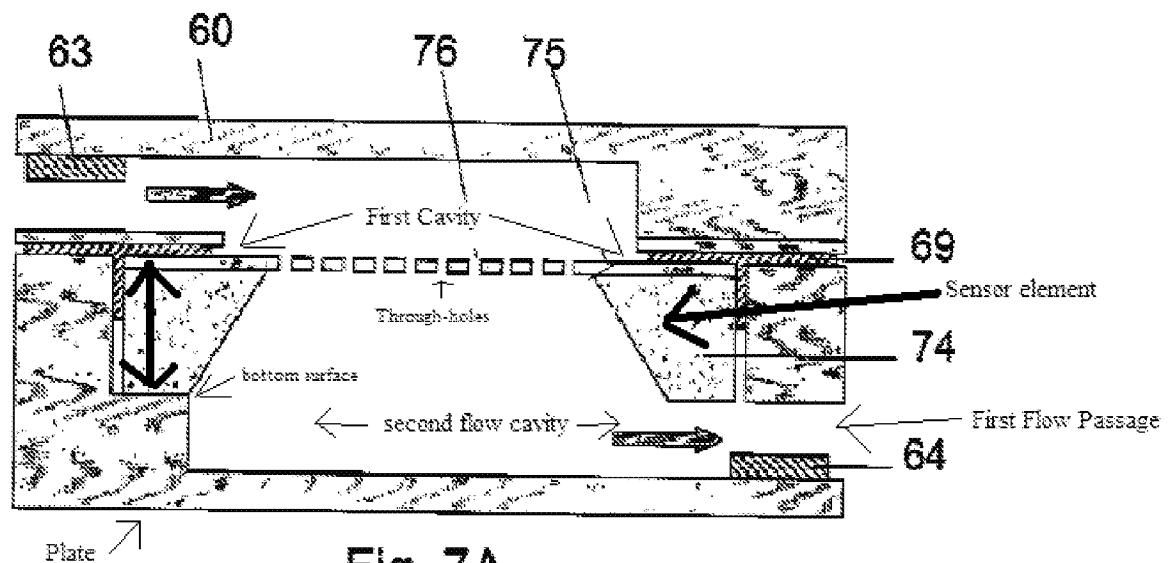
This is the second action on the merits.

Claims 1-5, 7-19 and 34-43 are pending in this application. Claims 6 and 20-33 are cancelled. Claims 1-5, 7-19 and 34-43 are amended. No new matter has been added.

### *Claim Rejections - 35 USC § 102*

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Claim 40 is rejected under 35 U.S.C. 102(b) as being anticipated by BECH et al (2002/0063067), from here on in referred to as BECH.

Concerning Claim 40, BECH teaches a device for electrophysiological measurements best exemplified by figure 7A shown below, which comprises the following features:



- A plate

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- A first cavity, said cavity having a bottom surface
- A second flow cavity in the claimed position
- A first flow passage, with first and second openings, the first opening into the second flow cavity and the second to the outside of the figure
- A sensor element being the same height as the first cavity, the bottom being flush with the bottom surface of the first cavity
- A through-hole allowing communication with the outer surface of the plate
- The first flow passage coupled in such a way as to inherently allow a sucking device to be attached.

***Claim Rejections - 35 USC § 103***

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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5. Claims 1-5, 10, 13-15, 17, 34 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over BECH, in view of BULLEN et al., (US 2003/0132109) from here on referred to as BULLEN.

Concerning Claim 1, BECH teaches a Figure 8 which shows a device with the following:

- a plate 60 with an upper surface (not defined by number)
- the plate having a first cavity 78 and 77 provided in the surface having a bottom surface (not numbered)
- a second cavity 82 in the bottom of 78 and 77.
- a first flow passage provided connecting 81 with cavity 82, the first opening, occurring at 81, the outside of the plate and the second opening, occurring at 82.
- a sensor element 74 provided in the cavity created by 78 and 77, which is further detailed in Figure 7A, the sensor element having:
  - a thin plate 75 with a first surface and a second surface (not defined by number) which has a plurality of through-holes 76 provided therein. These through-holes have a first opening and a second opening and communication between the two openings. Thin plate 74 separates cavity 78/77 and 82, and allows communication between 82 and the second opening of 76.
- a supporting substrate (not identified by number) under 77/78 and extending next to reservoirs 79 and 81.

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- the first flow passage connecting 82 with 81, which is an electroosmotic pump, analogous to the claimed sucking device and allowing for fluid flow in the first flow passage.

BECH does not expressly teach the limitations of a measuring stick, nor does BECH expressly teach a tube connected with the openings of the measuring stick and extending along it.

However, BULLEN teaches the use of a pipette for performing a patch-clamping method (abstract) best exemplified by figure 3. Specifically, BULLEN teaches an assembly 20' which comprises a guard pipette 60 (a stick) and a bubble pipette 20 (a tube). Differential pressure in the pipette 20 would lead the clamping of a cell at aperture 24.

At the time of the invention, it would have been prima facie obvious to those of ordinary skill in the art to use the pipette of BULLEN to modify the device of BECH to yield the claimed invention because known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_\_, \_\_\_, 82 USPQ2d 1385, 1395 – 97 (2007) (see MPEP § 2143, F.). In the present case, the distinguishing measuring stick and tube connected to the support of the claimed invention is very similar to what is already common use in single patch clamp methods using pipettes such those like BULLEN. The device of BULLEN is already configured to be manipulated by the user in a manner such that single cells in solution may be picked by

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hand while only having to submerge the tip of the device. This established use of BULLEN's invention would have prompted those of ordinary skill in the art to couple said invention with that of BECH in such a way so as to retain that functionality.

Therefore, the advantages of these design features, which are lacking in BECH, would have been obvious to include for one of ordinary skill in the art in light of previous patch clamping technology, even though the fields of pipette patch clamping and planar patch clamping may be considered different.

Concerning Claim 2, BECH in view BULLEN teach all the limitations of claim 1. Further, BECH teaches in Figure 8 how thin plate 75 sits flush with the rest of sensor element 74 which is integrally connected with the rest of the substrate, and therefore constitutes the bottom of cavity 77.

Concerning Claim 3, BECH in view BULLEN teach all the limitations of claim 2. Further, BECH teaches the surfaces of the supporting substrate (not identified by number) referred to in the rejection of claim 1 are presented in identical fashion to the claimed invention in Figure 8, with the bottom of the first cavity established with the surface of the supporting substrate.

Concerning Claim 4, BECH in view BULLEN teach all the limitations of claim 1. Further, BECH refers to this embodiment as having "housing 60," which contain these flow paths. Even though "plate" and "substrate" are never explicitly defined, the housing 60 can be considered the complexing of all structural elements, meaning that the plate analogues around above 77 and the substrate analogues around 78 and 82 can be considered bonded together, possible by the use of adhesive like in 69 of 7A.

Concerning Claim 5, BECH in view BULLEN teach all the limitations of claim 1. Further, BECH teaches in Figure 8 a second flow path connecting 81 with 82 in which the first opening allows flow to 82 and second opening opens to 81 and the outside of the plate.

Concerning Claims 10 and 17, BECH in view BULLEN teach all the limitations of claim 5. Further, BECH teaches in figure 8 a bump formed in the bottom of cavity 82 which corresponds to the bump 17 in cavity 6.

Concerning Claim 13, BECH in view BULLEN teach all the limitations of claim 1. Further, BECH teaches Figure 7A, which shows two electrodes 63 and 64 positioned around the first and second openings of the through-holes 76.

Concerning Claim 14, BECH in view BULLEN teach all the limitations of claim 1. Figure 7A shows how the legs of 74 create a pocket on the side encompassing the second openings of the through-holes 76 which is necessarily larger than that of the through-holes.

Concerning Claim 15, BECH in view BULLEN teach all the limitations of claim 1. Further, BECH teaches page 3, paragraph 0022, which discloses that the "first canal" may be made of glass.

Concerning Claim 34, BECH in view BULLEN teach all the limitations of claim 1. Further, BECH teaches a second flow passage which connects 82 with 79, an electroosmotic pump in the bottom of a reservoir, and is therefore necessarily suited to hold and pump a fluid.



Concerning Claim 37, BECH in view BULLEN teach all the limitations of claim 1. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to have the stick and tube of BULLEN extending from the device of BECH. The device of BULLEN is already configured to be manipulated by the user in a manner such that single cells in solution may be picked by hand while only having to submerge the tip of the device. This established use of BULLEN's invention would have prompted those of ordinary skill in the art to couple said invention with that of BECH in such a way so as to retain that functionality.

Concerning Claim 38, BECH in view of BULLEN teaches all the limitations of claim 1.

BECH does not expressly teach a measuring stick and tube in which the tube extends the entire length of the stick.

However, BULLEN shows in figure 3 a tube and stick configuration that the concentric tube and stick are of equal length.

At the time of the invention, it would have *prima facie* obvious to one of ordinary skill in the art to fashion the combined device of BULLEN and BECH in this fashion because known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_, \_\_, 82 USPQ2d 1385, 1395 – 97 (2007) (see MPEP § 2143, F.).

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Concerning Claim 39, BECH in view of BULLEN teach all the limitations of claim

1. Further, BECH teaches the first flow passage connects 82 with 81, which is an electroosmotic pump, analogous to the claimed sucking device and allows for fluid flow in the first flow passage.

6. Claim 7 rejected under 35 U.S.C. 103(a) as being unpatentable over BECH in view of BULLEN as applied to claims 1-5, 10, 13-15, 17, 34 and 37-39 above, and further in view of ROTTER et al (US 2,366,654), from here on in referenced as ROTTER.

BECH teaches a microfluidics device in Figure 8 with the limitations of claim 1 (see claim 1 rejection above).

BECH does not expressly disclose a valve between the reservoirs and flow passages and his device.

However, ROTTER discloses claim 1, which is a pump containing multiple valves.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the pump of BECH to include a valve such as any found in ROTTER or the like because known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_\_, \_\_\_, 82 USPQ2d 1385, 1395 – 97 (2007) (see MPEP § 2143, F.). In the present case, while a pump does not

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necessitate the use of a valve, the concept of pairing a valve with a pump is not novel, and therefore the claimed invention is obvious.

7. Claims 8, 11, 16, 18-19 rejected under 35 U.S.C 103(a) as being unpatentable over BECH in view of BULLEN as applied to claims 1-5, 10, 13-15, 17, 34 and 37-39 above, and further in view of FISHMAN al (2003/0032946), from here on in referenced as FISHMAN.

Concerning Claims 8 and 11, BECH in view of BULLEN teaches all the limitations of claim 5.

Modified BECH does not appear expressly disclose that the flow passages be greater than  $0.01\text{mm}^2$  in cross-sectional area.

However, FISHMAN discloses both Figures 7A and 7B, which teaches a microfluidic device with induced fluid flow [0014], such fluid necessarily compatible with cellular material. Both figures are endowed with flow passages 80 and 82 communicating with cavities 78 and 36 and an aperture 24 which can contain a membrane 42 (Figure 4). These flow passages each be capable of accepting "24 gauge Teflon hoses" [0120]. "24 gauge" is equivalent in size to a diameter of .58 mm, which yields a cross-sectional area greater than the claimed  $.01\text{mm}^2$ .

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to fashion the microchannels of modified BECH in the size as taught by FISHMAN because the sectional area of a flow passage, and by extension the fluid flow characteristics in the passage, is considered a result effective variable and the variation of said variables is a matter of obvious engineering design choice.

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Concerning Claim 16, BECH in view of BULLEN teach all the limitations of claim

1. Further, BECH teaches page 3, paragraph 0022, which discloses that the "first canal" may be made of glass.

Modified BECH does not appear to expressly disclose that the thin plate of the sensor element be capable of transmitting visible light.

However, FISHMAN discloses a device which can be monitored using confocal microscopy (page 13, paragraph 0118, lines 6-7). This is a test that necessitates a translucent device or surface, (see US 3,013,467 Figure 1D).

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the thin plate of modified BECH to include the translucency of FISHMAN because modified BECH would benefit greatly from being to monitor the effectiveness of the other major features of his invention, namely the ability to manipulate cells for the purposes of patch clamping.

Concerning Claim 18, BECH in view of BULLEN teach all the limitations of Claim 1.

Modified BECH does not appear to expressly disclose that the first flow surface of the thin plate of the sensor element 74 be flush with plate.

However, FISHMAN discloses figure 1C, which shows layer 16 flush with layer 18.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the sensor element with FISHMAN as this configuration is obvious to try. There are a limited amount of possible configurations of the thin plate

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on the plate and this configuration would be an obvious design choice at any stage of development for its possible implications with respect experimental results and manufacturing ease.

Concerning Claim 19, modified BECH in view of FISHMAN teach all the limitations of claim 18. Further, BECH discloses a Figure 8, in which the parallel orientation of the plates, evident from the parallel orientation of the components in that figure. Finally, BECH discloses feature 14, a cavity in layer 12, a portion of thin plate 74 from Figure 7A, which reads on the claimed third cavity.

Concerning Claim 35, BECH in view of BULLEN teach all the limitations of claim 15. Further, BECH teaches page 3, paragraph 0022, which discloses that the "first canal" may be made of glass.

Modified BECH does not appear to expressly disclose that the whole of the plate be capable of transmitting visible light.

However, FISHMAN discloses a device which can be monitored using confocal microscopy (page 13, paragraph 0118, lines 6-7). This is a test that necessitates a translucent device or surface, (see US 3,013,467 Figure 1D).

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the plate of modified BECH to include the translucency of FISHMAN because modified BECH would benefit greatly from being to monitor the effectiveness of the other major features of his invention, namely the ability to manipulate cells for the purposes of patch clamping.

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Concerning Claim 36, BECH in view of BULLEN teach all the limitations of claim 15. Further, BECH teaches page 3, paragraph 0022, which discloses that the "first canal" may be made of glass.

Modified BECH does not appear to expressly disclose that the whole of the plate be capable of transmitting visible light.

However, FISHMAN discloses a device which can be monitored using confocal microscopy (page 13, paragraph 0118, lines 6-7). This is a test that necessitates a translucent device or surface, (see US 3,013,467 Figure 1D).

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the plate of modified BECH to include the translucency of FISHMAN because modified BECH would benefit greatly from being to monitor the effectiveness of the other major features of his invention, namely the ability to manipulate cells for the purposes of patch clamping.

8. Claims 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over BECH in view of BULLEN as applied to claims 1-5, 10, 13-15, 17, 34 and 37-39, and further in view of TAYLOR et al ("...Turbulence in Curved Pipes," *Proceedings of the Royal Society of London*, 1929), from here on in referenced as TAYLOR.

Concerning Claim 19, modified BECH teaches all the limitations of claim 5.

Modified BECH does not expressly disclose the shape of the flow passages, which appear to only be straight.

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However, TAYLOR discloses in a summary on page 1 of his publication that "a higher speed of flow is necessary to maintain turbulence in a curved pipe than in a straight one."

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the straight flow path of BECH with a curved flow path, since curved flow paths were shown in TAYLOR to increase the flow velocity required for turbulent flow. One of ordinary skill in the art would have sought to avoid turbulent flow in the use of these devices, since turbulent flow can create bubbles in the flow passages which apart from possibly causing blockages in the passages, have been shown to be detrimental to similar electrical cellular experiments (e.g. electroporation) due to the possibly of "arcing" in the sample. Arcing can lead to a decrease in cellular viability and may cause loss of the sample.

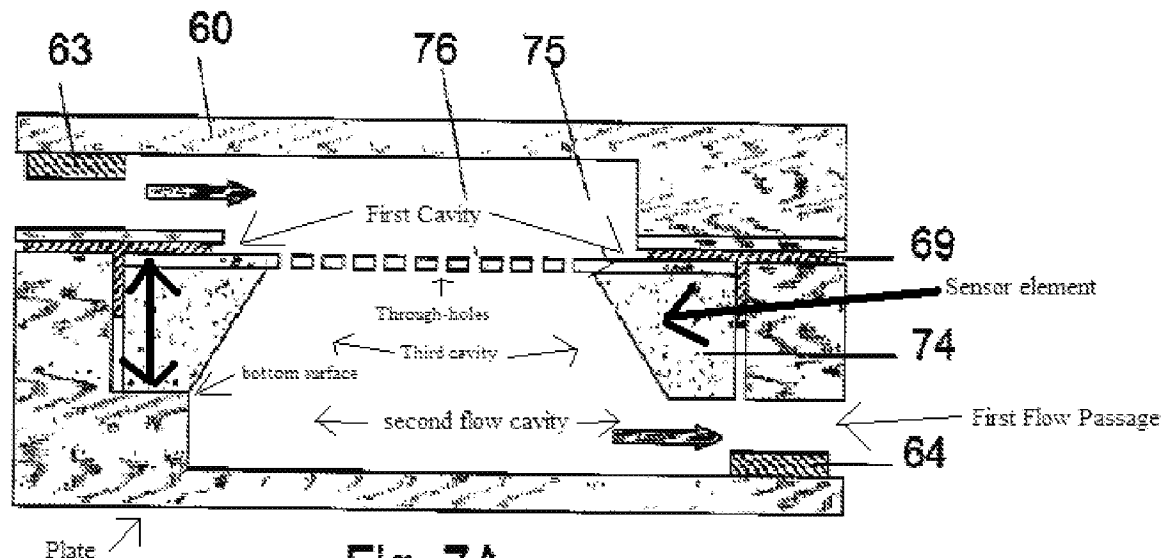
Claims 41-43 rejected under 35 U.S.C 103(a) as being unpatentable over BECH.

Concerning Claim 41-42, BECH teaches all the limitations of claim 40. Further, BECH teaches electrodes 63 and 64 positioned on either side of the sensor element.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to provide the electrodes of BECH in the claimed arrangement because the rearrangement of parts in a prior art device, when there is reasonable anticipation of success, is a matter of design choice is obvious over the prior art (MPEP 2144.04, VI, C).

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Concerning Claim 43, BECH teaches all the limitations of claim 40. Further, BECH teaches the following figure 7A, modified by examiner:



The figure teaches all the limitations of claim 40 and further teaches a third cavity provided in the upper surface of the sensor element, as well as through-holes being provided in the thin-plate.

At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to provide the sensor element in such a way that the thin-plate would be provided in the bottom of the sensor element, essentially the opposite of the prior part figure above. Creating the claimed invention would require only that the sensor element of the above figure be turned upside-down. The change in form or shape, without any new or unexpected results, is an obvious engineering design. See *In re Dailey*, 149 USPQ 47 (CCPA 1976) (see MPEP § 2144.04).



***Response to Arguments***

9. Applicant's arguments with respect to claims 1-5, 7-19 and 34-43 have been considered but are moot in view of the new ground(s) of rejection.

***Conclusion***

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT KASTEN whose telephone number is

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(571)270-7598. The examiner can normally be reached on Mon-Thurs, 8am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Sines can be reached on 571-272-1263. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/R. K./  
Examiner, Art Unit 1795

/Brian J. Sines/  
Supervisory Patent Examiner, Art Unit 1795